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RESEARCH PAPERS

Keratinocyte growth factor is required for hair development but not for wound healing

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Keratinocyte growth factor (KGF), also known as fibroblast growth factor 7 (FGF7), is synthesized by skin fibroblasts. However, its mitogenic activity is on skin keratinocytes, where it is the most potent growth factor identified thus far. To explore KGF's function in vivo, we used embryonic stem cell technology to generate mice lacking KGF. Over time, their fur developed a matted appearance, very similar to that of the rough mouse, whose recessive mutation maps at or near the KGF locus on mouse chromosome 2. In contrast to the recently reported transforming growth factor-alpha (TGF-alpha) and FGF5 knockouts, which showed defects in the follicle outer-root sheath and the hair growth cycle, respectively, the hair defect in the KGF knockout seemed to be restricted to the cells giving rise to the hair shaft. Thus, we have uncovered a third, and at least partially nonoverlapping, growth factor pathway involved in orchestrating hair follicle growth and/or differentiation. Surprisingly, the absence of KGF resulted in no abnormalities in epidermal growth or wound healing. This was true even when we engineered double knockout mice, null for both KGF and TGF-alpha, two factors that are increased dramatically in the normal wound-healing process. Whereas we found no evidence of compensatory changes at the mRNA level of wounded knockout mice, these data imply that the regulation of epidermal growth is complex and involves a number of growth stimulatory factors that go beyond what are thought to be the major paracrine and autocrine growth factors. We suggest that the redundancy in epidermal growth and wound healing is likely to stem from the vitality of these functions to the organism, a feature that is not a consideration for the hair follicle.

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